REMARKS

Claims 1-28 and 30-43 were pending in the present application. Claims 1-27 and 30-42 have been withdrawn from consideration. Please note that claim 43, which was added in the amendment filed on March 3, 2003, was incorrectly identified as claim 39 at that time. In the claims listed above and throughout this amendment, the previously incorrectly identified claim 39 will be correctly identified as claim 43.

Claims 28 and 43 (previously identified incorrectly as claim 39) were variously rejected under 35 U.S.C. § 112, first and second paragraphs.

By this amendment, claims 28 and 43 have been amended without prejudice or disclaimer of any previously claimed subject matter and new claims 44-49 have been added. Support for the amendments and new claims can be found, *inter alia*, throughout the specification. Support for the amendment to claim 28 can be found, *inter alia*, on page 8, lines 9-12. Support for the new claims 44-47 can be found, *inter alia*, in originally filed claims 8-11. Support for new claim 48 can be found, *inter alia*, in the specification on page 11, lines 16-18. Support for new claim 49 can be found, *inter alia*, in the specification on page 12, lines 10-11, and page 15, lines 15-28.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants thank the Examiner for acknowledging withdrawal of the previous rejections under 35 U.S.C. §§ 101, 112, first and second paragraphs, and 102(b) and withdrawal of the previous objections.

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. §112, second paragraph

Claims 28 and 43 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

Applicants thank the Examiner for suggested claim language and, although Applicants believe that the claims were sufficiently definite when considered in view of the specification and the understanding of those of skill in the art, Applicants have attempted to respond to the concerns of the Examiner in order to enhance clarity and to facilitate disposition of the present case.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C. §112, first paragraph

Claims 28 and 43 were variously rejected under 35 U.S.C. §112, first paragraph. Claims 28 and 43 were rejected as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention (i.e., lack of written description). Claims 28 and 43 were rejected for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims (i.e., scope of enablement). Applicants respectfully traverse these grounds for rejection.

The amended claims are directed to a process for the production of vitamin B_{12} comprising culturing a *Propionibacterium* host cell containing a polynucleotide comprising a sequence that is: a) SEQ ID NO:1 or the complement thereof; (b) a sequence that corresponds to

either the 1.7 kb SalI-AlwNI fragment of SEQ ID NO:1 or nucleotides 1 to 1800 of SEQ ID NO:1; or c) a sequence that is at least 70% homologous to a sequence as defined under (a) or (b) over a region of at least 100 contiguous nucleotides and which retains the ability to autonomously replicate in *Propionibacterium*.

Thus, all of the alternative sequences now claimed provide the polynucleotide with the ability to autonomously replicate in *Propionibacterium*.

In the written description rejection, the Examiner states that the "vast majority of such [claimed] plasmids would be unable to encode a vitamin B_{12} biosynthetic gene as they lack any functional replication origin and would thus be lost on growth of the bacterial culture." The Examiner asserts that "one cannot reasonably conclude that Applicants had possession of the attributes and features of all the claimed methods." Office Action, page 6. Applicants respectfully submit that this is not the case.

The specification exemplifies use of a polynucleotide with the sequence of SEQ ID NO: 1, in particular nucleotides 1 to 1800 of SEQ ID NO: 1. The specification also envisages and teaches homologous variants of those sequences (for example, at page 4, lines 14 to 17) and specifies that those variants may maintain the capability to autonomously replicate in *Propionibacteria* (for example, at page 8, lines 9 to 12). Once provided with the sequence of SEQ ID NO: 1, its function, and the specification, it is a relatively simple matter for a skilled person to create or identify homologous sequences as claimed which nevertheless retain replicative function.

With regard to the sequences of claim 28 part (c), Applicants respectfully submit that, at the time the application was filed, a skilled artisan would readily be able to identify and/or test a given sequence for the claimed features in part (c). For example, a simple sequence comparison will determine whether the sequence has 70% homology to SEQ ID NO: 1 over at least 100 contiguous nucleotides. In addition, biochemical assays for autonomous replication of a polynucleotide in a cell are described and exemplified in the specification (for example, in Examples 6 and 9) and are also well-known in the art.

The specification provides a description of sufficient, relevant, identifying characteristics of the claimed polynucleotides that one skilled in the art would recognize that the inventor had possession of the claimed invention when the application was filed. Applicants respectfully submit that the specification in combination with that known in the art adequately describes possession of the claimed genus to one skilled in the art. Thus, the pending claims are fully described in the specification as filed and Applicants respectfully submit that the written description requirement has been met.

In the scope of enablement rejection, the Examiner asserts that the scope of the claim is not in accordance with the scope of enablement. In support of the position, the Examiner states that "Applicants failed to disclose a sequence of *Propionibacterium*, which is capable of providing for replication of a heterologous gene within *Propionibacterium*, wherein the sequence is other than that of SEQ ID NO: 1 or its fragment consisting of nucleotides 1-1800." The Examiner also states that "Applicants have failed to define what are the necessary structural features of nucleotides 1-1800 for SEQ ID NO: 1 that provide for its activity of an origin of replication in *Propionibacterium*." Office Action, pages 9-10.

The Examiner asserts that the "probability of success in making the claimed invention is very low, and the experimentation left to those skilled in the art improperly extensive and undue." Office Action, page 11. Applicants respectfully disagree with this assertion.

As described above, the specification demonstrates that nucleotides 1 to 1800 of SEQ ID NO: 1 are sufficient for maintain replicative function in *Propionibacterium*. Also as described above, the specification provides methods for testing replicative function of the claimed variant sequences of SEQ ID NO: 1. Once provided with the sequence of SEQ ID NO: 1, its function, and the specification, Applicants respectfully submit that making a variant of the sequence as claimed and testing for replicative function is a routine matter practised by the person of skill in the art.

Applicants respectfully disagree that a specific definition of the structural features of nucleotides 1-1800 for SEQ ID NO: 1 that provide for its origin of replication activity in

Propionibacterium is necessary to enable the claimed invention. A skilled person would be unlikely to test for replicative function by sequence analysis but, instead, would experimentally test whether a given polynucleotide is replicative in practice, e.g. whether the polynucleotide is stably maintained through several generations of *Propionibacterium*. Methods for such an experimental test are described in the specification and are known in the art. Therefore, Applicants respectfully submit that the precise structural definition of the origin of replication does not need to be known in order for the claimed sequences to be enabled.

Applicants note that the test for enablement is not whether a certain amount of experimentation is required to practice an invention, but rather whether the amount of experimentation is "undue." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Applicants respectfully submit that the specification has provided a reasonable amount of guidance to the skilled artisan with respect to the direction in which the experimentation should proceed and that the skilled artisan would be able to extend the teachings of the specification and the art to the polynucleotide sequences as claimed.

Applicants respectfully submit that the specification provides adequate guidance pertaining how to make and/or use the claimed polynucleotide sequences. Accordingly, the pending claims are in compliance with the enablement requirements.

In sum, Applicants submit that the pending claims fall within the subject matter that is enabled and described by the specification as filed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 251502009000. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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